

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

| |
|---------------------|
| FRIST: 22.10.05 |
| VORFRISTEN: 22.8.05 |
| AKTE: |
| NOT: <i>cr</i> |

PCT

To:

see form PCT/ISA/220

Geiss & Große

Patentanwälte Rechtsanwälte
Stuttgart

31. MRZ. 2005

Bearbeiter: *SG*

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/IB2004/004247

International filing date (day/month/year)
22.12.2004

Priority date (day/month/year)
22.12.2003

International Patent Classification (IPC) or both national classification and IPC
C07K14/505

Applicant
DUBAI GENETICS FZ-LLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Pinheiro Vieira, E

Telephone No. +49 89 2399-7865



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY****Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/004247

Box No. II Priority

1. ☐ The following document has not been furnished:

☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☒ The International Searching Authority has not been able to consider the validity of the priority claim because a copy of the earlier application whose priority has been claimed was not available to the International Searching Authority at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/004247

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 48,54-63

because:

☒ the said international application, or the said claims Nos. 48,54-63 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/004247

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|---------------|
| Novelty (N) | Yes: Claims | |
| | No: Claims | 1-64 |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-64 |
| Industrial applicability (IA) | Yes: Claims | 1-47,49-53,64 |
| | No: Claims | 48,54-63 |

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

III.1 Claims 48 and 54 -63 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

V Reasoned statement.

V.1 Cited documents.

- 1.1 D1: US-B1-6 221 608 (JOHNSON DANA ET AL) 24 April 2001 (2001-04-24)
D2: WENGER ROLAND H ET AL: 'Oxygen-regulated erythropoietin gene expression is dependent on a CpG methylation-free hypoxia-inducible factor-1 DNA-binding site' EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 253, no. 3, May 1998 (1998-05), pages 771-777, XP002283479 ISSN: 0014-2956
D3: MAXWELL P H ET AL: 'INDUCIBLE OPERATION OF THE ERYTHROPOIETIN 3' ENHANCER IN MULTIPLE CELL LINES: EVIDENCE FOR A WIDESPREAD OXYGEN-SENSING MECHANISM' PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 90, March 1993 (1993-03), pages 2423-2427, XP000827984 ISSN: 0027-8424
D4: EP-A-0 984 062 (CYTOS BIOTECHNOLOGY AG) 8 March 2000 (2000-03-08)
D5: EP-A-1 064 951 (HOFFMANN LA ROCHE) 3 January 2001 (2001-01-03)

- 1.2 D1 discloses a process for the production of erythropoietin binding protein in a medium containing 20% O₂ (see examples)

D2 and D3 concern the production of EPO by culturing cells at reduced partial pressure of oxygen.

D4 discloses the production of erythropoietin by culturing cells at 5% CO₂.

D5 concerns erythropoietin derivatives conjugated to polyethylene glycol.

V.2 Novelty (Art. 52(1) and 54 EPC).

- 2.1 The present application concerns a process for the preparation of erythropoietin (EPO) by providing a first and a second cell and culturing the cells under conditions (e.g. reduced partial pressure of oxygen) that induce EPO production, EPO proteins and its use in compositions a methods of treatment.
- 2.2 In the light of the prior art documents D1-D5 the subject matter in claims 1-64 is not novel (see also item 3.1 below).
- 2.3 The applicant should indicate in the letter of reply the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof.

V.3 Other objections.

- 3.1 Claims 42-48 are drafted as product by process claims. These type of claims is only allowable if the products (Erythropoietin) as such fulfil the requirements of patentability, i.e., inter alia that they are novel and inventive. Contrarily, Erythropoietin is neither novel nor inventive (see, e.g., the prior art documents D1-D5). Moreover, said claims are to be drafted as "product X obtainable by process Y" (see the Guidelines part C-III 4.7b).
- 3.2 Claim 64 lacks support and conciseness within the meaning of Art. 6 PCT as the number of diseases claimed is so vast and unrelated that is impossible to determine which is the effect obtained with the claimed compounds. Moreover, said claims lack disclosure within the meaning of Art. 5 PCT as the description does not offer sufficient teaching for the invention to be carried out by a person skilled in the art.